Examiner rejects the claims stating that first, claim 15 is not limited to any particular site of administration and second, the specification does not address the timing of admistering the nucleic acid. Office Action page 5. Additionally the Examiner states that the specification does not teach a dose range for the claimed method. Office Action pages 6, 7. Applicants respectfully traverse.

Applicants acknowledge the Examiner's initial concern regarding the administration site with respect to the claim 15. On 18 April 2002 Applicants amended claim 15 limiting administration to the wound site. Applicants also filed new claims 23-28. Using the same language, Applicants introduced the same administration site limitation in the newly filed claims. In the Office Action, the Examiner states that the issue of the administration site does not apply to claims 23-38, as they are "limited to direct administration to the wound site." Page 5. Given the similarity between the language of claim 15 and claim 23, Applicants believe that claim 15, like claim 23, does not raise an issue regarding the site of administration. Claim 15 is limited to direct administration to the wound site. Applicants request the rejection be withdrawn.

Regarding the Examiner's second issue, that the timing of the administration is not addressed, Applicants respectfully traverse the Examiner's rejection. Applicants submit that the timing of the administration is taught in the specification, that the timing of the administration as taught comports with what was known in the art, and that the method as described is embraced by language of the claims. Applicants suggest that clarification of the meaning of the term "wound site" used in the specification and claims may be helpful in addressing the Examiner's rejections.

As pointed out by the Examiner, at the time the application was filed, it was reported in the art that timing is important in the administration of compounds intended to beneficially affect cytokines in the wound healing process. Office Action Jan 18 2002 page 10. Applicants' cited references Shah et al. concludes that "reduction in scarring was achieved when the neutralizing antibody to TGF-B was administered early (days 0-2, 0-6, 1-7) but the best effects were seen when the treatment regime included the day of wounding, (i.e. day 0). This suggests that crucial events occur even immediately after injury."

Applicants were aware of the report in the art and its relevance to their study. Applicants cited the Shah study in the specification immediately after summarizing the conclusions of their own study. Specification Page 4. Applicants' study, Example 4, takes into account the timing issues reported in the art. In Example 4, polynucleotides encoding NAB1 and NAB2 were administered to rats at a wound site, prior to wounding, (i.e. "day 0"), and found reduced levels of TGF-B1 and increased levels of TGF-B3. Thus, Example 4 addresses the timing administration issue that was recognized in the art. The study takes into account what was reported in the art.

The claim language embraces the method as taught in Example 4. The Examiner suggests "the claims recite that the nucleic acid molecule is administered to a 'wound site of the mammal,' not to at site that will be a wound site. Consequently, administration of the nucleic acid molecule to a future wound site is not embraced by the claims." Office Action Page 6. Applicants respectfully disagree. The meaning of the term "wound site" includes both an existing wound site and a "site that will be a wound site" and is consistent with definition of other related terms used in the art including "incision site" "surgical site" and "administration site." These specific uses of the word "site" are likewise consistent with the use of "site" generally. The word "site" includes in its definition the location of an actual or planned object or event. Thus, Applicants' use of the term "wound site" in the claims embraces the administration of the nucleic acid at a wound site prior to wounding, such as disclosed in Example 4.

As explained above, the issue of timing of the administration is addressed in the specification. The timing of the administration as taught in the specification comports with what was known in the art at the time of filing. The method as described is embraced by language of the claims. Therefore, Applicants respectfully request the rejection be withdrawn.

The Examiner states that "the specification is devoid of teaching on the amount of NAB1 or NAB2 protein per amount of tissue at a wound site required to reduce scarring" and that it does not teach "how the amount of nucleic acid used in [*in vitro*] experiments relates to treating a mammal." Office Action page 6. As stated in the Amendment of 18 April 2002, Applicants have provided a range of potential doses typical in the art.

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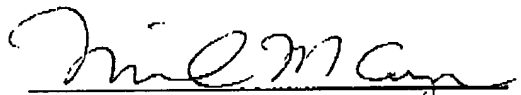
Applicants believe the specification provides sufficient guidance to allow one skilled in the art to practice the invention. One skilled in the art can determine specific dosage without undue difficulty or experimentation. Applicants request the rejection be withdrawn.

Applicants submit that the claims are in condition for allowance and request favorable reconsideration.

Respectfully Submitted,



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